Assessment of Cardiovascular Regulation After Burns by Nonlinear Analysis of the Electrocardiogram

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Critical illness and hypovolemia are associated with loss of complexity of the R-to-R interval (RRI) of the electrocardiogram, whereas recovery is characterized by restoration thereof. Our goal was to investigate the dynamics of RRI complexity in burn patients. We hypothesized that the postburn period is associated with a state of low RRI complexity, and that successful resuscitation restores it. Electrocardiogram was acquired from 13 patients (age 55 ± 5 years, total body surface area burned 36 ± 6%, 11 ± 5% full thickness) at 8, 12, 24, and 36 hours during postburn resuscitation. RRI complexity was quantified by approximate entropy (ApEn) and sample entropy (SampEn) that measure RRI signal irregularity, as well as by symbol distribution entropy and bit-per-word entropy that assess symbol sequences within the RRI signal. Data (in arbitrary units) are means ± SEM. All patients survived resuscitation. Changes in heart rate and blood pressure were not significant. ApEn at 8 hours was abnormally low at 0.89 ± 0.06. ApEn progressively increased after burn to 1.22 ± 0.04 at 36 hours. SampEn showed similar significant changes. Symbol distribution entropy and bit-per-word entropy increased with resuscitation from 3.63 ± 0.22 and 0.61 ± 0.04 respectively at 8 hours postburn to 4.25 ± 0.11 and 0.71 ± 0.02 at 24 hours postburn. RRI complexity was abnormally low during the early postburn period, possibly reflecting physiologic deterioration. Resuscitation was associated with a progressive improvement in complexity as measured by ApEn and SampEn and complementary changes in other measures. Assessment of complexity may provide new insight into the cardiovascular response to burns. (J Burn Care Res 2008;29:56–63)

Burns are associated with significant cardiovascular changes. Cardiac output decreases in response to increased afterload, decreased plasma volume, and myocardial depression.[1,2] In some nonburn models, both direct microneurographic recordings[3,4] and indirect assessment of autonomic nervous system (ANS) activity by means of heart-rate variability (HRV) analysis[5,6] have provided useful insights into how the ANS responds to hypovolemia. However, studies applying these techniques to burn patients are scarce.

Among the tools suitable for assessment of HRV are frequency-based techniques such as fast Fourier transform[7] and complex demodulation (CDM).[8] These techniques quantify respectively the strength (power) and amplitude of periodic oscillations in the heart rate, ie, in the R-to-R interval (RRI) of the electrocardiogram (ECG). They are based on assumptions of linear proportionality in physiologic responses to stimuli. The respiratory sinus arrhythmia is one such periodic oscillation, which takes place in synchrony with the respiration. This is considered a high-frequency oscillation. Other oscillations, taking place at lower frequencies, are also present in the RRI. High-frequency oscillations are predominantly the

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result of vagus nerve input to the heart. On the other hand, low-frequency oscillations are the combined result of both vagus and sympathetic nerve inputs to the heart.[9] The ratio of low-to-high-frequency modulations of the RRI is a proposed index of the relative contributions of the sympathetic and vagal systems to heart-rate control. This index has been termed "sympatho-vagal balance."[10] A high ratio suggests high sympathetic activity relative to vagal activity, whereas a low ratio suggests the opposite.[7]

Newer techniques of HRV analysis involve nonlinear statistical methods. These methods account for nonlinear physiologic responses to stimuli, that reflect interacting and mutually modulating processes. Rather than attempt to dissect out the relative contributions of high-frequency and low-frequency oscillations in the heart rate, these methods quantify the amount of irregularity or complexity in the ECG signal. Numerous studies have demonstrated that the healthy heart rate is characterized by a certain level of complexity, and that disease, as well as normal ageing, are characterized by a decrease in such complexity.[11–14] We previously applied both frequency-domain and nonlinear techniques to the analysis of ECG during hemorrhagic shock and found that hypovolemia leads to a decrease in RRI complexity, paralleled by a decrease in high-frequency power (HF). With resuscitation, complexity and HF were restored.[15]

The purpose of this study was to characterize the cardiovascular response to burns and resuscitation by means of nonlinear and frequency-domain analysis of the ECG. We hypothesized that the early postburn period is associated with a decrease in heart-rate complexity and an increase in sympatho-vagal balance, and that resuscitation leads to restoration of these values.

METHODS

This study was approved by the Institutional Review Board of Brooke Army Medical Center, Fort Sam Houston, Texas, and was conducted at the U.S. Army Institute of Surgical Research (U.S. Army Burn Center).

Patient Selection

ECG waveform data collected in the burn unit from 27 patients admitted for burn resuscitation on another ongoing research protocol were screened for the study. Patients were excluded from the study if the following criteria were not met: 1) ECG of 800 RRI in length was available for analysis at the required timepoints; and 2) ectopic beats were present within the analyzed data segments, based on the modified Brooke formula.[1] Fluid infusion rates were adjusted based on the urine output.

ECG Analysis

The ECGs of 13 patients were continuously monitored from the time of admission, were digitally recorded at 500 Hz to a computer throughout the first 2 days postburn, and were stored for off-line analysis at a later timepoint. The ECGs were semiautomatically analyzed by an operator who was blinded to any aspects of patient care. Information obtained during our study was not available for decision making by the providers. ECG analysis was conducted at four discrete timepoints: upon admission (an average of 8.31 ± 0.35 hours after burn (hour 8), as well as at 12, 24, and 36 hours after burn. For each timepoint, 800-beat sections of ECG were imported into WinCPRS software (Absolute Aliens Oy, Turku, Finland). Eight hundred beats were used consistently because the variables calculated (approximate entropy [ApEn] in particular) are affected by the number of R waves in the dataset.[16] Automatic identification of R waves was performed by the software, and manually verified. The software generated the instantaneous RRI time series (ie, the beat-to-beat RRI as a function of time), and variables were calculated as described previously.[15,17] The following are the main variables which were calculated.

Frequency-Domain Techniques

Fast Fourier Transform

1. Total power: reflects the strength of periodic oscillations within the RRI signal throughout the entire power spectrum.
2. Low-frequency component of the RRI power spectrum, or low-frequency power (LF): influenced by both sympathetic and vagal activity.
3. HF: influenced by vagal activity.
4. LF/HF ratio: reflects sympatho-vagal balance, ie, the relative contributions of the sympathetic and vagal modulations to the heart.
5. The LF and HF were normalized by dividing the LF and HF spectra by the total power. This yielded normalized powers (LFnu, HFnu). These values may provide a better picture of autonomic activity than the non-normalized values.[7] All values reported are normalized values.

Complex Demodulation. The method of CDM provides continuous assessment of the amplitude of high- and low- frequency fluctuations in the RRI.[18]

1. CDM LF: a measure of the amplitude of low-frequency fluctuations in the RRI.

2. CDM HF: a measure of the amplitude of high-frequency fluctuations in the RRI.
3. CDM LF/ CDM HF: reflects sympatho-vagal balance, ie, the ratio of the amplitudes of sympathetic-to-vagal influences on the heart.

Nonlinear Analysis Techniques

1. Approximate entropy and sample entropy (SampEn): measure the amount of irregularity in the RRI signal.[17] ApEn determines the conditional probability of finding specific patterns in the time series, ie, the logarithmic likelihood that a run of patterns that is close remains close on the next incremental comparison. The template patterns are constructed from the signal itself, and no a priori knowledge of the system is needed. SampEn is a similar concept to ApEn, with the computational difference that the vector comparison with itself is removed.
2. Fractal dimension by curve lengths (FDCL): measures the degree to which the RRI time series resembles a fractal, ie, possesses self-similarity at multiple scales. A section (curve) of the signal is conceptualized as consisting of a number of short segments. FDCL counts the number of such segments of various lengths needed to follow the curve of the signal. For the fractal dimension by dispersion analysis (FDDA), a new signal is created from the means of sets of two adjacent values in the original signal. Groups (m) of adjacent data points (4, 16, etc.) are used. The Log SD (m) is plotted against log m. FDDA is defined as 1-slope. FDDA has values between 1 (constant signal) and 1.5 (maximally fractal or random signal).[17]
3. Detrended fluctuations analysis (DFA): determines fractal-like correlation properties and uncovers short- and long-range (power-law) correlations within the signal.[19] Briefly, the RRI time series is segmented into short boxes of a certain length. The degree of dispersion of the data from the linear trend within each box is calculated as the sum of squares of the residuals after subtraction of the linear regression line (detrending). Totals of residuals from consecutive boxes are calculated for short[4–10] or longer segments of RRI intervals. In this study we explored the short-term scaling exponent by DFA.
4. Similarity of distributions (SOD): explores the probability of similar RRI signal amplitude distributions as a function of time.[20]
5. Symbol-dynamics indices: symbol distribution entropy (SymDis), percentage of forbidden words (FW), and bit-per-word entropy (BPWEn): collectively measure the probability of patterns within the RRI time series, which is encoded in symbols.[21] Namely, SymDis is based on recreation of the dynamics of a complex system in phase space by coarse graining.[21] The phase space is divided into sections of RRI ± 2 SD of the normal-to-normal RRI and ± 1 SD of normal-to-normal RRIs. Each possible location within these four regions is encoded as symbols 0 to 3, creating four possible locations within the phase space. The order in which the dynamics of the system visits the possible encoded regions creates a symbol distribution sequence, SymDis. Symbol sequences are encoded into words (2–3 symbols in length). The frequency of occurrence of each word is then counted and the normalized entropy (BPWEn) of these words is calculated from a histogram. If the probability of a word sequence is $<.001$ the word is considered forbidden. The number of FW is counted as a percentage.
6. Signal stationarity (StatAv): assesses whether the mean and standard deviation of the signal changes over time during each data set.[22]

In addition, baroreflex sensitivity was calculated in the time domain by the sequence method.

Statistical Analysis

Repeated-measures analysis of variance was performed using SAS version 9.1 (SAS Institute, Cary, NC) to compare changes in variables compared to admission values. Data are presented as means ± SEM. When appropriate, non-normally distributed data were logarithmically transformed before statistical analysis. A P value of $<.05$ was considered indicative of statistical significance.

RESULTS

ECG waveforms from 27 patients were screened. After exclusion of 14 patients, ECGs from 13 patients (nine men and four women) were used in this study. The mean age of the patients was 55 ± 5 years; weight 85 ± 6 kg; total body surface area (TBSA) burned 36 ± 6%; and 11 ± 5% full thickness. Three subjects had inhalation injury. All but three subjects survived to hospital discharge. One patient died 2 days after admission due to cardiopulmonary arrest, and the two other patients died 61 and 126 days after admission both due to multiorgan failure (MOF) and sepsis. Ten patients received mechanical ventilation (eight, high-frequency percussive ventilation; one, airway pressure release ventilation; and one, synchronized intermittent mandatory ventilation with pressure support). Pain control was accomplished with fentanyl and midazolam in nine pa-

Table 1. Resuscitation and urine output

Variable	Hour 8	Hour 12	Hour 24	Hour 36	*P* 8 vs 12	8 vs 24	8 vs 36
Resuscitation (ml/kg)	68.44 ± 11.59	110.22 ± 23.43	205.11 ± 40.83	257.96 ± 46.32	<.001	<.001	<.001
Resuscitation (ml/kg/TSBA)	2.13 ± 0.46	3.16 ± 0.58	5.94 ± 1.03	7.51 ± 1.10	<.001	<.001	<.001
Urine output (ml/kg/hr)	0.53 ± 0.15	1.10 ± 0.30	0.69 ± 0.09	1.51 ± 0.49	.1448	.4401	.0574
Urine output (ml/hr)	69.23 ± 22.91	78.15 ± 25.32	51.54 ± 5.74	117.77 ± 28.53	.5096	.7447	.1392

tients with periodic morphine administration as needed in the other four. Two patients (one of them an eventual nonsurvivor that developed MOF) received vasoactive medications throughout the study.

Heart rate and blood pressure did not change significantly during resuscitation. Cumulative results of fluid resuscitation and hourly urine output are summarized in Table 1. The total volume infused during the first 24 hours postburn was 5.94 ± 1.03 ml/kg/TBSA burned.

Frequency-domain results are presented in Table 2. Changes in these metrics were not significant. Baroreflex sensitivity did not change.

Nonlinear results are provided in Table 3. Measures of complexity (ApEn and SampEn) were both low at hour 8. These metrics increased in concert, reaching values (1.22 ± 0.04 for ApEn) at hour 36 similar to those described for ambulatory individuals[23]; see also Figure 1. FDDA increased at hour 12. FDCL did not change. The short-term fractal correlations within the RRI as measured by DFA were high at hour 8 compared with normal values (DFA = 1 for healthy individuals). Subsequent changes in DFA were insignificant at hours 24 and 36. SOD decreased at hour 12. FW and StatAv both decreased at hour 12. BPWEn and SymDis both increased significantly at hour 24 (Table 3).

DISCUSSION

This report introduces the use of RRI analysis as a tool for improving our understanding of heart-rate control during the early postburn period. There were 2 principal findings: 1) a state of low RRI complexity, as measured by ApEn and several other complementary but computationally different nonlinear metrics, characterized patients during early postburn period; 2) postburn resuscitation led to progressive increases in RRI complexity, reaching normal levels at 36 hours. These changes all occurred in the absence of changes in the heart rate or blood pressure.

Nonlinear Analyses as Markers of Physiologic Status

Physiologic signals such as the heart rate are inherently complex and dynamic, and feature irregular patterns of complex variability. This structural complexity of the signal is a consequence of mutual interactions of cardiac control with other organ systems (eg, the respiratory sinus arrhythmia), and of multiple cause-effect relationships featuring nonlinear behavior.[24–26] In a nonlinear system, a change in one input variable may lead to disproportionate changes in the other component variables; these changes may be described by nonlinear functions involving products and powers.[14,25,27,28]

Table 2. Frequency-domain and complex demodulation analysis results

Variable	Hour 8	Hour 12	Hour 24	Hour 36	*P* 8 vs 12	8 vs 24	8 vs 36
RRI	614.31 ± 46.35	596.69 ± 35.65	646.31 ± 35.25	598.46 ± 35.30	.89	.59	.92
BRS	347.70 ± 199.39	365.50 ± 197.57	344.06 ± 192.32	203.35 ± 125.25	.94	.90	.94
LF	0.59 ± 0.10	0.56 ± 0.08	0.47 ± 0.07	0.51 ± 0.08	.96	.21	.50
HF	0.38 ± 0.09	0.42 ± 0.08	0.48 ± 0.06	0.43 ± 0.07	.82	.41	.89
LF/HF	4.42 ± 1.29	3.36 ± 1.09	1.41 ± 0.27	2.10 ± 0.59	.92	.30	.24
CDM LF	9.61 ± 3.14	8.62 ± 2.66	7.00 ± 2.05	7.15 ± 1.97	.68	.24	.40
CDM HF	5.23 ± 1.18	4.77 ± 1.05	6.62 ± 1.42	6.00 ± 1.55	.95	.40	.80
CDM LF/CDM HF	1.63 ± 0.35	1.63 ± 0.30	0.93 ± 0.14	1.24 ± 0.23	.76	.17	.78

Table 3. Nonlinear analysis results

Variable/Timepoint	Hour 8	Hour 12	Hour 24	Hour 36	P 8 vs 12	P 8 vs 24	P 8 vs 36
ApEn	0.89 ± 0.06	1.08 ± 0.06	1.18 ± 0.05	1.22 ± 0.04	.03	.0010	.0003
SampEn	0.83 ± 0.08	1.11 ± 0.08	1.26 ± 0.07	1.29 ± 0.07	.01	.0005	.0003
FDCL	1.69 ± 0.04	1.73 ± .04	1.78 ± 0.02	1.78 ± .03	.57	.09	.09
FDDA	1.12 ± 0.03	1.22 ± 0.03	1.18 ± 0.03	1.19 ± 0.04	.02	.23	.15
DFA	1.39 ± 0.13	1.38 ± 0.09	1.13 ± 0.10	1.16 ± 0.08	.99	.07	.18
SOD	0.20 ± 0.04	0.15 ± 0.01	0.17 ± 0.03	0.17 ± 0.02	.03	.29	.49
FW	55.92 ± 2.92	45.08 ± 4.93	46.62 ± 3.77	46.69 ± 2.92	.046	.19	.06
BPWEn	3.63 ± 0.22	4.15 ± 0.19	4.25 ± 0.11	4.13 ± 0.11	.11	.03	.10
SymDis	0.61 ± 0.04	0.69 ± 0.03	0.71 ± 0.02	0.69 ± 0.02	.11	.03	.10
StatAv	0.83 ± 0.05	0.67 ± 0.06	0.74 ± 0.04	0.73 ± 0.07	.04	.39	.30

Nonlinearity is an intrinsic feature of the cardiovascular system,[14,16,28] that results in RRI irregularity.[29] Thus, the *structural complexity* of the RRI may be a reflection of the *regulatory complexity* of its underlying control system.

In the current study, complexity was measured by several computationally different techniques. From a practical standpoint, the entropy methods—ApEn and SampEn—quantify structural differences within the RRI signal over time. Via assessment of the randomness within the signal, they point to predictability of the next pattern within the signal.[17] If the probability of a repetitive pattern in the signal is high, the signal is deemed regular and low in entropy, which may imply a decreased amount of regulatory feedback. In this study, the postburn period was characterized by a low entropy state as measured by ApEn and SampEn at 8 hours, suggesting a considerable decrease in the amount of cardiovascular regulation.

This loss of complexity could signify more simple control of the system in response to immediate, life-threatening stress with "prioritization" of vital control mechanisms. Alternatively, disassociation of regulatory interconnectedness between organ systems may also be a possible mechanism for decreased complexity.[26,30] Our observation that resuscitation restored complexity to values similar to those seen in ambulatory persons (ApEn of about 1.2)[23] is new and may be clinically significant, pending further verification in larger cohorts. Buchman suggested that restoration of functional interconnectedness between organ systems may be an important target for therapy[30]; the current study may provide evidence of the effectiveness of resuscitation in restoring regulatory complexity—but the exact mechanisms are, at this point, unclear.

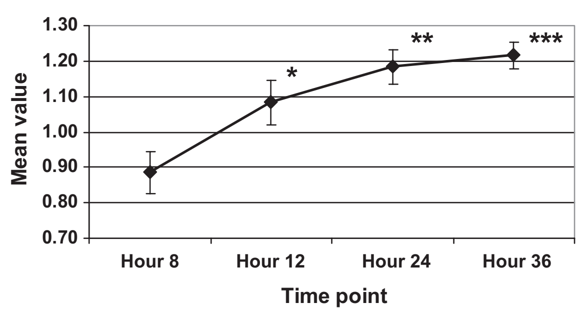

Figure 1. Changes in complexity as measured by ApEn during postburn resuscitation. Timepoint hour 8 denotes admission to the burn intensive care unit (mean time 8.4 hours after injury). Timepoints Hour 12, Hour 24, Hour 36 show respective times after burn in hours. Asterisks denote significant changes vs baseline (*$P < .05$, **$P < .005$, ***$P < .001$). Arbitrary units.

Our current data are consistent with our previous findings in a swine model of survivable hemorrhagic shock, in which complexity as measured by ApEn and SampEn decreased with blood loss and was restored with resuscitation.[15] Using the same metrics, in a model of severe hemorrhagic shock in sheep we also observed a decrease in RRI complexity that returned to baseline levels with resuscitation.[6] We also found in prehospital trauma patients that a state of decreased RRI complexity differentiated eventual nonsurvivors from survivors.[31] Thus, the current findings of decreased complexity during postburn period and restoration with resuscitation are consistent with other work and build growing confidence in the potential use of nonlinear metrics as "new vital signs" that reflect changes in cardiovascular regulatory complexity during critical illness.

Complexity is also reflected in the fractal organization of the RRI signal. A fractal is a structure which is self-similar regardless of scale.[32] This means that provided a suitable magnification, shorter sections of the RRI are similar in structure to longer sections. The increase in FDDA at 12 hours points to increased RRI signal fractality with resuscitation which is important in the context of a comprehensive assessment of improvement in signal dynamics. A signal that is more fractal in structure is more complex and more richly regulated. One of the more powerful nonlinear tools is detrended fluctuation analysis (DFA), which measures the self-similarity of fractal processes by quantification of the short- and long-term correlations in the data.[19] Normal RRI signals feature a certain amount of such correlations, which render the overall dynamics of the system to be neither completely random nor completely organized, with a normal DFA value of 1. Deviations from this value in either direction are abnormal. In this study the short-term correlations in the RRI signal were increased (1.39), implying abnormal cardiovascular regulation at hour 8 postburn, but showed a trend (nonsignificant changes) toward normalization of the values at hour 24 and 36. In the work of others, abnormal DFA predicted increased length of stay in the intensive care unit after coronary grafting[33]; our findings are therefore consistent with literature indicating an association between abnormal RRI correlations and critical illness.

SOD is a method that explores the probability of similar RRI signal amplitude distributions as a function of time.[20] SOD decreased in association with resuscitation at hour 12, signifying an increase in irregularity of RRI signal distribution and thus a state of higher complexity at hour 12 when compared to hour 8. In our previous work, nonsurviving prehospital trauma patients had a mean SOD value of 0.28 whereas survivors had a significantly lower value at 0.19.[31]

The symbol-dynamics indices are generated by a process which converts the RRI signal to a sequence of symbols that represent the dynamics of the signal in phase space over time.[21] In our study, the FW showed a decrease at 12 hours, pointing to a decrease in the percentage of pathological patterns (low probability locations within the phase space) in the signal and a trend toward normal values in the signal dynamics with resuscitation. BPWEn and SymDis measures increased at hour 24. These findings are consistent with our previous results, in which the symbol-dynamics indices decreased with hemorrhagic shock and were restored with resuscitation.[15] Others have reported on decreases in the symbol dynamics measures during hypotension in dogs.[22] Because the symbol-dynamics measures are computationally distinct from the other nonlinear measures used in this study, the uniformity of the changes with the other metrics explored in this study lends additional confidence to the results.

Assessment of signal stationary is an important goal during waveform analysis because data nonstationarity undermines the reliability of the frequency-domain analysis techniques. Nonstationary signals are those in which the mean and standard deviation change during the course of a data set (ie, at a given time point) as can be expected in real-life unstable patients. StatAv is a measure of stationarity that assesses the baseline shifts of the signals; it is higher with less stationary signals.[22] StatAv at the early postburn period (0.83) was similar numerically to values documented by us in prehospital trauma patients (0.82).[31] In this study StatAv decreased at hour 12 but did not change thereafter, showing that early resuscitation increased StatAv.

Frequency-Domain Analysis

Frequency-domain measures (such as fast Fourier transform) and CDM quantify the strength of the periodic oscillations in the RRI, and may provide information about the effect on the RRI of specific branches of the ANS. The HF of the RRI, which measures oscillations at the respiratory rate, is related to vagal cardiac activity. The LF of the RRI, which measures oscillations at a slower rate, is affected by both vagal and sympathetic cardiac activity.[7,34] The ratio of low-to-high-frequency oscillations has been proposed as an index of the balance of sympathetic to vagal cardiac control. One would expect a high sympatho-vagal balance to be a reflection of autonomic compensation postburn which would be likely to decrease with restoration of volume. In the current study observed decreases in sympatho-vagal balance as measured by both LF/HF and CDM LF/CDM HF were not significant. Previously, we observed an increase in sympatho-vagal balance during progressive hemorrhagic shock.[6] Lack of significance in the frequency-domain results, in the present study, may be explained by the lower sensitivity of these methods to dynamically changing conditions.

Autonomic correlates for the complexity metrics are not yet clearly defined in the literature although both we[6,15] and others[22] have shown unidirectional changes in complexity measured by ApEn and vagal modulation of the heart as measured by the HF component of the frequency domain analysis. Thus, we speculate that the autonomic adjustments postburn may, at least in part, involve restoration of vagal influences on the heart.

Perspective

This study is the first that applies linear and nonlinear analysis of ECG to burn patients. Until additional prospective studies in large patient cohorts are completed using a variety of ECG waveform analysis techniques, we recommend exploration of multiple methods during the search for new vital signs. This approach will ensure both complementary information as well as increase the reliability of the findings. To date, however, both animal and human data suggest that the entropy-based estimates of complexity (ApEn, SampEn), the fractal correlation metric DFA, and the SOD respond most consistently to hypovolemia and resuscitation.

Evaluation of RRI complexity can be done noninvasively, in real time and with minimal requirements for computing power, once the relevant analytic algorithms are incorporated to a computer chip or PDA—thus making it a potentially useful tool for remote monitoring.

In the three patients that eventually succumbed to their injuries, initially diminished levels of complexity at admission to the hospital (mean 0.82) were not different from the other patients within the investigated cohort (mean 0.83) This, however, is not surprising considering that two out of the three died 61 and 126 days after admission due to MOF. The one nonsurvivor that died hours after our last analysis points died abruptly due to cardiopulmonary arrest. The time-resolution of the nonlinear analysis techniques in forecasting sudden cardiac death is under active exploration. Thus, the monitoring, prognostic and diagnostic value of complexity analysis is promising but remains to be explored in large, well selected cohorts.

Finally, loss of functional interconnectivity and regulatory loss between organ systems has been proposed as a possible mechanism in pathogenesis of multiple system organ failure.[26] Nonlinear measures have been used to track the return of such interconnectivity following successful cardiac transplant.[35,36] A more complete understanding of the effect of burns and resuscitation on RRI complexity—and of the potential utility of this approach in patient care—will require a larger sample size, stratified by age, burn size, and outcome. Until then, we speculate that the current study may be an example of one of the physiological benefits of resuscitation as a way of restoring the integrity of cardiovascular regulatory pathways in patients with burns.

Limitations

This retrospective analysis of ECGs in burn patients undergoing resuscitation was conducted on "clean" ECGs that were free of ectopy. This approach is common to HRV analysis at present. Other techniques will be needed to exploit the information content of ectopic beats.[37] All of the metrics involved in this study are influenced to some extent by the effects of analgesia, sedation, and mechanical ventilation.

CONCLUSION

Loss of RRI complexity characterized patients after burns, and resuscitation led to improvements in RRI complexity by hour 36 to levels which are seen in normal individuals. Improvements in complexity with resuscitation were demonstrated by several computationally distinct statistical methods. Evaluation of cardiovascular regulatory complexity may be useful for patient monitoring. Prospective, large-scale clinical trials are warranted and will help determine the clinical utility of various metrics derived from RRI analysis.

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